DRAFT
Report on Carcinogens
Substance Profile for

Glass Wool Fibers (Respirable) as a Class

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This DRAFT substance profile contains the NTP's preliminary recommendation on the listing status of glass wool fibers in the Report on Carcinogens, summarizes the scientific information that supports the recommendation, and provides information on use, exposure, and production as well as any existing federal regulations.

This draft is distributed solely for the purpose of public comment and predissemination peer review and should not be construed to represent final NTP determination or policy.

Additional information about the NTP Report on Carcinogens review process for candidate substances is available at http://ntp.niehs.nih.gov/go/29353.

Revised June 4, 2010

Glass Wool Fibers (Respirable) as a Class

CAS No.: None assigned

Reasonably anticipated to be a human carcinogen

First listed in the *Seventh Annual Report on Carcinogens* (1994)

Carcinogenicity

Respirable glass wool fibers as a class are reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity in experimental animals and supporting mechanistic evidence.

Glass wool fibers are fine glass fibers forming a mass resembling wool, commonly used for insulation or filtration. Respirable fibers are those that can penetrate into the alveolar region of the lung upon inhalation; in humans, a fiber with an aerodynamic diameter of less than 5 μm is respirable (EPA 2001). Aerodynamic diameter, unlike geometric diameter, takes into account fiber density and aspect ratio (ratio of length to diameter). The World Health Organization defines respirable fibers as less than 3 μm in diameter and over 5 μm long, with an aspect ratio of at least 3:1 (WHO 2000).

Carcinogenicity within the class of respirable glass wool fibers varies, and not all fibers within this class cause cancer. A spectrum of responses was observed in experimental animal studies; for example, some glass wool fibers were carcinogenic by several routes of exposure, including inhalation; some were carcinogenic only by routes of exposure other than inhalation; and some were not carcinogenic in any studies. Studies in experimental animals demonstrated a greater carcinogenic effect for special-purpose fibers (see "Use" section below for definition) than for the respirable fraction of glass fibers typically used as insulation wools.

The potential for exposure to glass wool fibers to cause cancer is influenced by dose, fiber dimensions (length and diameter), chemical composition, and biopersistence within the lung (see "Fiber Properties and Mechanisms Related to Carcinogenicity"). Although the end uses of respirable glass wool fibers vary, the physicochemical properties and sizes of fibers used in various applications overlap. For example, insulation wool fibers typically have nominal diameters of 1 to 10 μm, and special-purpose fibers have nominal diameters of 0.1 to 3 μm, although individual diameters can vary around the nominal diameter, so that a product with an average diameter of 5 μm can contain fibers with diameters ranging from less than 1 to over 20 μm (ACGIH 2001, IARC 2002). Because of the overlap in physicochemical properties, no quantitative distinction can be made with respect to carcinogenic potential based on commercial application (e.g., special-purpose vs. insulation). At present, no single physicochemical property or set of properties measured *in vitro* (e.g., dimensions, chemical constituents, surface chemistry) of glass wool fibers can adequately predict the carcinogenic potential of a specific fiber *in vivo*. Commercial products with the same use may have different compositions. The European Commission and Germany have standardized *in vivo* testing of fibers for carcinogenicity and issued criteria for classifying the carcinogenicity of synthetic vitreous fibers; however, to date, *in vitro* carcinogenicity testing has not been standardized. Thus, the carcinogenicity of individual glass wool fibers must be evaluated

on a case-by-case basis until the properties that lead to development of cancer after inhalation exposure are more clearly defined.

Studies of Cancer in Experimental Animals

Glass wool fibers caused tumors in two rodent species, at several different tissue sites, and by several different routes of exposure. Several types of glass wool fibers were studied in chronic carcinogenicity bioassays in rats and/or hamsters exposed by a number of routes, including inhalation, intratracheal instillation of fiber suspensions, surgical intrathoracic implantation, and direct exposure to the pleural or peritoneal cavity by injection. Administration of glass wool fibers by each of these exposure routes caused tumors in at least one study. Testing employed various glass wool products and treated or sized fractions of the products. Inhalation exposure studies used respirable fibers as defined by WHO criteria unless otherwise specified.

The most biologically relevant studies were of inhalation exposure to respirable fibers in rats and hamsters. Because of technical limitations (e.g., lack of sensitivity of the bioassay, poor respirability of fibers, and particle overload), negative findings from inhalation exposure studies conducted before 1988 (NTP 2009) are not informative for this assessment. Although intratracheal instillation (a bolus injection into the trachea) bypasses the upper respiratory airway, exposure by this route also is relevant to human exposure. Intrathoracic, intrapleural, and intraperitoneal exposures are less relevant biologically; however, studies using these routes do provide information about the cancer hazard of glass wool fibers. Studies of the carcinogenicity of glass wool fibers following chronic exposure, described below, are organized by fiber use (special-purpose, insulation, unspecified, or experimental) and route of exposure.

Special-Purpose Glass Fibers

The majority of studies that found carcinogenic effects of glass wool fibers tested special-purpose fibers. Most of the studies used type 475 glass fibers; one study tested E-glass fibers; and one tested a series of unspecified special-purpose fibers. Type 475 glass fibers are coded according to mean fiber diameter, with larger numbers indicating larger diameters (e.g., Johns Manville [JM] 110/475 fibers have a greater nominal diameter [1.9 to 3.0 μm] than JM 100/475 fibers [0.28 to 0.38 μm]). Man-made vitreous fiber (MMVF) 33 is a mixture of respirable fibers of type 475 glass codes 104, 108B, and 110.

Inhalation exposure to E-glass fibers significantly increased the incidences of lung cancer (carcinoma) and total lung tumors (carcinoma and adenoma) in male Wistar rats; mesothelioma was found in two animals (Cullen *et al.* 2000).

Inhalation exposure to MMVF 33 glass fibers caused mesothelioma in a male Syrian golden hamster but no lung tumors. Although only one hamster developed mesothelioma, it was believed to be exposure-related because of (1) the high incidence of fibrosis, mesothelial hypertrophy, and mesothelial hyperplasia of the pleura in other exposed hamsters, (2) the rarity of the spontaneous occurrence of this type of tumor, and (3) the presence of glass fibers in the thoracic wall and diaphragm (McConnell *et al.* 1999, Hesterberg *et al.* 1997). Inhalation exposure of F344 rats to two sizes (average diameter of < 3.5 μm and length of either < 10 μm or > 10 μm) of Tempstran code 100/475 glass fibers without binder and to Owens-Corning FM Series Air Filter Media with binder (average diameter of 0.5 to 3.5 μm and length of > 10 μm) significantly

increased the incidence of mononuclear-cell leukemia in rats (males and females combined). Although F344 rats have a high spontaneous incidence of mononuclear-cell leukemia, these findings were considered to be exposure-related because of the presence of granulomatous pleural and subpleural plaques and glass-laden macrophages in adjoining lymph nodes. It is possible that mediators of the inflammatory response or the fibers directly could transform cells in this strain, which has a high spontaneous incidence of neoplasia (Moorman *et al.* 1988, Mitchell *et al.* 1986). Inhalation exposure of Wistar rats to JM 100/475 glass fibers did not cause lung tumors or mesothelioma (Davis *et al.* 1996, Cullen *et al.* 2000).

Intratracheal instillation of JM 104/475 glass fibers significantly increased the incidences of lung tumors (adenoma, adenocarcinoma, and squamous-cell carcinoma) in female Wistar rats (Pott *et al.* 1987) and thoracic tumors (carcinoma of the lung, mesothelioma, and thoracic sarcoma) in one of two studies in male Syrian hamsters (Pott *et al.* 1984b, Feron *et al.* 1985). In female Osborne-Mendel rats administered eleven types of unspecified special-purpose glass fibers by intrathoracic implantation, the incidence of mesothelioma was significantly increased for seven of the types of glass fiber (compared with the incidence in a control group implanted with autoclaved gelatin-saturated coarse fibrous glass vehicle comparable in weight to the test fibers plus vehicle) (Stanton *et al.* 1977, 1981). Intrapleural or intratracheal injection of type 475 glass fibers (codes 100, 104, or 110) caused mesothelioma in rats (Sprague-Dawley, Wistar, or Osborne-Mendel) (Wagner *et al.* 1976, Monchaux *et al.* 1981, Pott *et al.* 1987, Smith *et al.* 1987, Wagner *et al.* 1984). Sarcoma and unspecified tumors also were observed in rats administered type 475 glass fibers by intraperitoneal injection (Pott *et al.* 1984b, Muhle *et al.* 1987, Miller *et al.* 1999).

Insulation Glass Fibers

Types of insulation glass wool fibers tested in experimental animals included Owens-Corning glass wool, MMVF 10 and 10a (both of which represent the respirable fraction of Manville 901 glass fiber), MMVF 11 (the respirable fraction of CertainTeed B glass fiber), and unspecified glass wool fibers.

Inhalation exposure of F344 rats to ~~two types of~~ Owens-Corning FG Insulation Fiberglass with binder ~~glass wool~~ (4 to 6 μm in diameter and > 20 μm long~~ or 0.5 to 3.5 μm in diameter and > 10 μm long~~) significantly increased the incidence of mononuclear-cell leukemia in rats (males and females combined); as with the findings for Tempstran code 100/475 glass fibers in this strain (discussed above), these findings were considered to be exposure-related (Mitchell *et al.* 1986, Moorman *et al.* 1988). Inhalation exposure to MMVF 10 and 11 glass fibers did not cause lung tumors or mesothelioma in F344 rats (Hesterberg *et al.* 1993); MMVF 10a did not cause tumors in male Syrian hamsters (McConnell *et al.* 1999 and Hesterberg *et al.* 1997). Intrathoracic implantation of two unspecified types of insulation glass wool fibers in female Osborne-Mendel rats resulted in mesothelioma in one animal from each group; incidences were significantly different from the unexposed controls but not the vehicle implant controls (Stanton *et al.* 1977, 1981). Intraperitoneal injection of MMVF 11 glass fibers caused mesothelioma of the abdominal cavity in male and female Wistar rats (Roller *et al.* 1996, 1997), and intraperitoneal injection of MMVF 10 glass fibers increased tumor rates in male Wistar rats (Miller *et al.* 1999).

Fibers with Unspecified Commercial Applications

For Schleicher and Schuell (S&S 106) and borosilicate glass wool fibers, information on commercial applications is not clear. Intraperitoneal injection of S&S 106 glass fibers in female Wistar rats caused dose-dependent increases in the incidences of mesothelioma and combined tumors (mesothelioma and spindle-cell sarcoma) (Pott 1976a). No tumors were observed following intratracheal instillation of borosilicate glass wool in rats (Schepers 1974), guinea-pigs (Schepers 1974, Kuschner and Wright 1976), or rabbits (Schepers 1974).

Experimental Fibers

Male and female Wistar rats injected intraperitoneally with B-1, B-09, or B-20 glass fibers (Roller *et al.* 1996, 1997) and female Wistar rats injected with the biosoluble glass wool fibers B, P, and V developed mesothelioma in the abdominal cavity, but no tumors were observed in animals injected with M glass wool fibers (Grimm *et al*. 2002).

Fiber Properties and Mechanisms Related to Carcinogenicity

Early studies of the relationship between glass wool fiber properties and carcinogenicity demonstrated a relationship between tumor incidence and fiber size or shape (Stanton *et al.* 1977, 1981, Pott 1989, Pott *et al.* 1984a, 1987, 1991, Muhle *et al.* 1987, Roller *et al.* 1996, 1997, Lambré *et al.* 1998, Miller *et al.* 1999, Cullen *et al.* 2000, Adachi *et al.* 2001, Grimm *et al.* 2002). Inhalation exposure studies showed that tumor incidence or the severity of the lesion increased with the dose of fibers in the lung (Bunn *et al.* 1993, Hesterberg *et al.* 1993, 1995, 1997, 1999, McConnell 1994, McConnell *et al.* 1999). Fiber dimensions and durability also were found to be important determinants of tumorigenicity: long, thin fibers are associated with greater tumor incidence.

Biopersistence (the ability of a fiber to remain in the lung) is a critical factor in assessing a fiber's carcinogenicity within the alveolar environment, as it takes into account physical properties of the fiber (such as solubility) and the physiological clearance by the tissue. In a study with female Wistar rats, biopersistence was measured by the half-time of the fiber in the lung, and cancer pathogenesis was assessed. Most of the tested fibers longer than 20 μm with a high *in vitro* fiber dissolution rate (K_{dis}) at pH 7.4 and low biopersistence had low carcinogenic potency (Lambré *et al.* 1998). Bernstein *et al*. (2001a,b) reported that biopersistence clearance half-time was a good predictor of both the collagen deposition (fibrosis) observed in chronic inhalation and intratracheal instillation studies and the tumor response observed in intraperitoneal injection studies. ~~In a study with female Wistar rats, biopersistence was measured by the half-time of the fiber in the lung, and cancer pathogenesis was assessed. Fibers longer than 20 μm with a high K_{dis} at pH 7.4 and low biopersistence had low carcinogenic potency (Lambré *et al.* 1998). Bernstein *et al*. (2001a) reported that biopersistence clearance half-time was a good predictor of both the collagen deposition (fibrosis) observed in chronic inhalation and intratracheal instillation studies and the tumor response observed in intraperitoneal injection studies.~~

A mathematical model relating the K_{dis} to fiber carcinogenicity and fibrosis provided evidence that K_{dis} values at pH 7.4 could be used to predict tumorigenicity for inhalation exposure ($P = 0.16$, chi-square test, no significant disagreement between the

model and the data) (Eastes and Hadley 1996); the dissolution constant was inversely related to tumorigenicity. However, a clear threshold value of K_{dis} for the prediction of fiber carcinogenicity is not known or standardized. Dissolution-constant testing has not been standardized across laboratories, and different research groups have reported different K_{dis} values for the same fiber (Zoitos *et al.* 1997). K_{dis} can be measured at two different pHs (7.4 and 4.5), and it is unclear which assay conditions are the most relevant to carcinogenicity (Guldberg *et al.* 1998). However it is unclear whether dissolution rate can accurately predict the carcinogenicity of a specific fiber. For example, although the reported K_{dis} for the respirable insulation fiber MMVF 10 (122.4 ng/cm^2 per hour) was higher than that for the special-purpose fiber JM 100/475 (9.1 ng/cm^2 per hour), the incidence of mesothelioma in rats exposed by intraperitoneal injection was higher for the insulation fiber (59%) than for the special-purpose fiber (33%) (Miller *et al*. 1999). Fiber dissolution is not the sole factor contributing to biopersistence. As of 2010, no regulatory agency in the United States or the European Union had adopted the dissolution constant as a predictor of fiber carcinogenicity.

Fiber properties such as dose, dimensions, chemical composition, and surface reactivity determine whether a fiber can be effectively engulfed by an alveolar macrophage and efficiently cleared from the lungs or remain and cause a chronic inflammatory response (Nguea *et al.* 2008). If fibers are too long for the macrophage to effectively engulf or are too durable to break or dissolve within the lung or macrophage environment, incomplete phagocytosis can result in excessive production and release of reactive oxygen species (ROS) and inflammatory mediators into the lung, which can lead to chronic inflammation and fibrosis (Hesterberg and Hart 2001). Fibers not cleared by macrophages can also be taken up by lung epithelial cells and translocated to the pleural space, resulting in chronic inflammation of the pleural and mesothelial membranes, tissue damage, cell proliferation, and fibrosis (Oberdörster 2002). An increase in malondialdehyde, a biomarker for oxidative stress, but no increase in mutation frequency, was reported in rats following intratracheal exposure to glass wool (Topinka *et al*. 2006). Culturing primary rat alveolar cells with glass fibers induced the proinflammatory cytokine tumor necrosis factor–alpha through activation of both mitogen-activated protein (MAP) kinase and nuclear factor–kappaB (NF-κB) gene transcription pathways (Ye *et al.* 1999, 2001). These pathways can be activated by ROS. In these studies, long fibers (16.7 ± 10.6 μm) were more potent than short fibers (6.5 ± 2.7 μm) in activating MAP kinases. MAP kinase and NF-κB are important factors in cell-signaling pathways controlling cell proliferation and cell death.

Glass wool fibers have the potential to cause genetic damage (Nguea *et al.* 2008). *In vitro,* they caused production of ROS in cell-free systems and oxidative damage in cell-culture systems. In cultured mammalian cells, they caused DNA damage, micronucleus formation, chromosomal aberrations, and DNA-DNA interstrand crosslinks (NTP 2009). Intratracheal instillation of insulation glass wool caused DNA strand breaks in rat alveolar macrophages and lung epithelial cells. Although fibers of various dimensions caused DNA damage in mammalian cells, longer fibers were more potent in causing these genotoxic effects (Topinka *et al.* 2006).

In cytotoxicity studies, longer fibers were more toxic than shorter fibers to rat alveolar macrophages (Hart *et al.* 1994, Blake *et al.* 1998). Exposure to glass wool fibers caused cytotoxicity and anchorage-independent growth in mouse fibroblasts;

amplification of the proto-oncogenes K-*ras*, H-*ras*, c-*fos*, and c-*myc*; and mutations in K-*ras* and *p53* tumor-suppressor genes (Gao *et al.* 1995, Whong *et al.* 1999). Exposure to glass wool fibers also caused cytotoxicity and morphological transformation in Syrian hamster embryo cell cultures (Hesterberg and Barrett 1984). Thick fibers (average diameter = 0.8 μm, average length = 9.5 μm) were 20-fold less potent than thin fibers of the same length (average diameter = 0.13 μm, average length = 9.5 μm) in causing cell transformation, and shorter fibers (average length = 1.7 μm, average diameter = 0.13 μm) were 10-fold less potent than longer fibers of the same diameter (average length = 9.5 μm, average diameter = 0.13 μm). Cytotoxic potencies of the fibers were associated with their transforming potencies. These results provide evidence that fibers can have direct cytotoxic and transforming effects on cells, and that the magnitude of the response is related to fiber dimensions.

Studies of Cancer in Humans

There is inadequate evidence of the carcinogenicity of glass wool fibers as a class from the available studies in humans. Although studies of occupational exposure found excess lung-cancer mortality or incidence, there was no convincing evidence that the excess lung cancer was due to exposure specifically to glass wool fibers, because (1) no clear positive exposure-response relationships were observed, and (2) the magnitudes of the risk estimates were small enough to potentially be explained by co-exposure to tobacco smoking.

The data relevant for evaluation of exposure specifically to glass wool fibers consist of a series of studies of four major cohorts of glass wool manufacturing workers in the United States (Marsh *et al.* 2001a,b, Youk *et al*. 2001, Stone *et al.* 2001, 2004), Europe (Boffetta *et al*. 1997, 1999), Canada (Shannon *et al.* 2005), and France (Moulin *et al*. 1986), and a hospital-based case-control study of lung cancer among Russian workers exposed to glass wool (Baccarelli *et al.* 2006). The most informative studies are the U.S. multi-plant cohort study and a nested case-control study of lung cancer within that cohort, because they (1) had adequate statistical power to detect an effect, as a result of the cohort's large size (> 10,000 male and female workers) and long follow-up period, (2) adjusted for tobacco smoking (in the nested case-control study of male workers), (3) used internal analyses to evaluate quantitative exposure to respirable fibers (using nonexposed workers in the cohort as the reference group), and (4) separated the results for women (the only study to do so). The French study was the least informative, because of its short follow-up period. The U.S. study reported mortality data, the French study reported incidence data, and the European and Canadian studies reported both mortality and incidence data. Respiratory cancer (including upper-respiratory-tract and lung cancer) and mesothelioma were the cancers of interest; the data were inadequate to evaluate cancer at other tissue sites. None of the studies clearly distinguished between glass wool used for insulation or for special-purpose applications.

Respiratory System Cancer or Lung Cancer

Excesses of respiratory cancer mortality or incidence were found in three of the four cohort studies (not adjusted for smoking) and the case-control study of Russian workers (adjusted for smoking); the fourth (French) cohort had limited statistical power to detect an effect because of the very small number (5) of cases among exposed workers.

Findings were statistically significant in the U.S. study (standardized mortality ratio [SMR] = 1.18, 95% confidence interval [CI] = 1.04 to 1.34, 243 exposed deaths, males and females, specific for glass wool plants) and the Canadian study (SMR = 1.63, 95% CI = 1.18 to 2.21, 42 exposed deaths; SIR = 1.60, 95% CI = 1.19 to 2.11, 50 exposed cases). A meta-analysis of the four cohorts yielded a summary relative risk (RR) that approached statistical significance (RR = 1.22, 95% CI = 1.00 to 1.49, 920 exposed cases). (The meta-analysis (Lipworth *et al.* 2009) used risk estimates for workers at both filament and glass wool plants in the U.S. study and mortality data for the Canadian and European cohorts.)

The association between cancer and exposure to glass wool fibers among males and females in the U.S. cohort was evaluated by internal analyses. The nested case-control study of lung cancer among male workers found no evidence of an association between working in plants manufacturing glass wool fibers and respiratory system cancer (lung, larynx, trachea, or bronchus) after adjusting for tobacco smoking (RR = 1.06, 95% CI = 0.71 to 1.6). In exposure-response analyses, no association was found between cumulative exposure or average intensity or duration of exposure to respirable glass fibers (Marsh *et al.* 2001a, Youk *et al.* 2001, Stone *et al.* 2001). In contrast to the findings for male workers, there was some evidence for an increased risk of respiratory-system cancer among female workers in glass wool plants (unadjusted RR = 3.24, 95% CI = 1.27 to 8.28) based on 6 cases in exposed workers (Stone *et al.* 2004). Employment duration and time since first employment were significantly related to respiratory cancer mortality, but no association was found with cumulative exposure to respirable fibers. Estimates were not adjusted for smoking, but a survey of smoking habits among a subset of workers found a slightly lower (24.5%) percentage of current smokers among workers than in the general population (29%). The meaning of the finding of a potential association with lung-cancer mortality among women, but not men, is unclear, because women had lower exposure than men. It is not known whether the elevated risk in women is (1) a false positive result due to the small number of exposed cases, (2) due to potential confounding from other occupational exposures, or (3) due to possibly greater susceptibility of women to lung cancer. The Russian hospital-based case-control study found higher risk estimates for workers exposed at higher levels, but no trends were found for cumulative exposure (Baccarelli *et al.* 2006).

Although the Canadian and European studies did not evaluate quantitative exposure to glass wool fibers, they did evaluate risk by employment duration and latency. No clear exposure-response patterns for lung cancer mortality were observed in either study, although an approximately threefold increase in mortality was observed among Canadian workers with over 20 years of employment duration and over 40 years since first exposure (Shannon *et al.* 2005).

Cancer of the Upper Respiratory and Alimentary Tract

Excesses of cancer of the upper respiratory tract and alimentary tract (oral cavity, pharynx, and larynx) were reported for the European cohort (SIR = 1.41, 95% CI = 0.80 to 2.28, 16 exposed cases) and French cohort (SIR = 2.18, 95% CI = 1.31 to 3.41, 19 exposed cases); risks increased with increasing exposure duration in the French cohort (Moulin *et al.* 1986) and time since first employment in the European cohort (P_{trend} = 0.03). Findings for these combined tissue sites were not reported in the Canadian study.

Excess mortality from buccal and pharyngeal cancer also was observed in the European study, but was not related to time since first employment or employment duration; no excess of buccal and pharyngeal cancer was observed in the U.S. study. A meta-analysis (Lipworth *et al.* 2009) using mortality data from the U.S. study (not including laryngeal cancer), and incidence data from the European study (not including laryngeal cancer) and the French study found an elevated but statistically nonsignificant risk for head and neck cancer (summary RR = 1.42, 95% CI = 0.91 to 2.1). The interpretation of these findings is unclear, because of limited exposure-response analyses and lack of adjustment for tobacco smoking.

Mesothelioma

The available data are inadequate to evaluate the association between glass wool exposure and mesothelioma, a rare cancer strongly linked to asbestos exposure. Mesothelioma was evaluated in detail only for the U.S. cohort; in the other studies, the reporting on mesothelioma either was not specific for exposure to glass wool fibers (Engholm *et al.* 1987, Rodelsperger *et al.* 2001) or did not evaluate co-exposure to asbestos (Boffetta *et al.* 1997). In the U.S. cohort, two cases of mesothelioma were identified among workers with exposure to glass wool but without known exposure to asbestos; in one case, there was uncertainty in the cancer diagnosis, and in the other case, information on asbestos exposure was not complete (Marsh *et al.* 2001b).

Properties

The chemical composition of glass wool products varies depending on the manufacturing requirement and end use, but almost all contain silicon dioxide as the single largest oxide ingredient (IARC 2002). Silicon dioxide or one of a few other oxides (boron trioxide, phosphorus pentoxide, and germanium dioxide) is required in order to form glass, and these oxides are known as "glass formers." The essential property of a glass former is that it can be melted and quenched into the glassy state. Commercial glasses generally include additional oxides that serve as stabilizers and modifiers or fluxes and modify the physical and chemical properties of the glass product, including viscosity, which is an important characteristic for fiberization (NTP 2009). These modifiers include oxides of aluminum, titanium, zinc, magnesium, lithium, barium, calcium, sodium, and potassium. In addition, various lubricants, binders, antistatic agents, extenders and stabilizers, and antimicrobial agents may be added to various glass wool products.

Glass wool consists of individual fibers, which have been basically defined since the late 1950s as being over 5 μm long and having a length-to-width aspect ratio of at least 3:1 (i.e., the fiber is at least three times as long as its width) (Walton 1982, Breysse *et al.* 1999). Other, more recent, definitions have suggested that an aspect ratio of 5:1 will more readily discriminate fibrous from irregularly shaped particles, and some organizations have adopted this criterion. Glass wool fiber diameters vary within a product but follow an approximately log-normal distribution. The fiber diameter is controlled by the manufacturing process. All glass fibers are manufactured to nominal diameters that vary based on the manufacturing process and the fibers' intended use (ACGIH 2001). The nominal diameter is an estimate of the product's average fiber diameter. Current glass wool production processes are not capable of producing fibers only at the nominal diameter; as a result, the diameters of individual fibers in a glass

wool product vary widely around the nominal diameter (IARC 2002). The manufacturing process also affects fiber length. In glass wool insulation, most fibers are several centimeters long; however, fibers break crosswise and lengths of less than 250 μm (considered by IARC as the upper limit of respirability) probably are present in all glass wool products (IARC 2002).

Fibers have also been classified based on other characteristics, including biopersistence, retention and clearance rates, and biodurability. The European Union and Germany have established criteria for labeling and classifying synthetic vitreous fibers (including glass fibers) based on their potential to be hazardous to human health, which is dependent both on a fiber's physical dimensions and its chemical composition.

Use

Glass fibers can generally be classified into two categories based on usage: (1) low-cost, general-purpose fibers typically used for insulation applications and (2) premium special-purpose fibers used in limited specialized applications. The primary use of glass wool is for thermal and sound insulation. The largest use of glass wool is for home and building insulation in the form of loose wool, batts (insulation in the form of a blanket, rather than a loose filling), blankets or rolls, or in the form of rigid boards for acoustic insulation. Glass wool is also used for industrial, equipment, and appliance insulation.

Special-purpose glass fibers are limited-production materials (~1% of total production) compared with insulation glass wool, and they are used for a variety of applications that require either a specialized glass formulation or particular diameter requirements. The largest market for special-purpose glass fibers is for battery separator media, i.e., the glass wool fibers physically separate the negative and positive plates in a battery, while allowing the acid electrolyte to pass through. Another important use is in high-efficiency particulate air (HEPA) filters that are used in settings where high-purity air is required. Aircraft, spacecraft, and acoustical insulation are also applications for special-purpose glass fibers.

Production

The major methods for fiber manufacture historically have been steam attenuation, the rotary or centrifugal process, and flame attenuation; only the latter two remain in use today, with the rotary process being the predominant method. In the production process, raw materials are first weighed and blended before being added to the fiberglass furnace, where the materials are melted and homogenized at approximately 1,370°C (2,500°F) (Wallenberger *et al.* 2001). In the rotary process, fibers are produced as centrifugal force extrudes the molten material through small holes in the side of the spinning device (Burgess 1995). The primary fibers pass through a circular burner flame, whose hot gases attenuate the fibers to their final diameter and break the fibers into shorter lengths, ultimately forming a veil of interlaced fibers that often are sprayed with a binder and lubricant (IARC 2002). A gas-fired oven dries the product and cures the binder.

A two-step flame-attenuation process is used to produce very small diameter fibers (IARC 2002). In the first step, the melt is drawn through the bushings of the furnace to produce strands of coarse fibers. The fibers are then remelted with a high-temperature gas

flame that attenuates the coarse fibers into finer fibers that are propelled through a forming tube.

In 2000, an estimated 3,388 million pounds (1.7 million tons) of fiberglass were used in building insulation with almost 81% being used in residential construction and 19% in commercial or industrial construction (Maxim *et al.* 2003). ATSDR (2004) reported Glass Manufacturing Industry Council (GMIC) data that indicated 10 major manufacturers were operating approximately 40 plants within the United States in 2002, and the production volume of all glass fiber types, including glass wool, was estimated at about 3 million tons annually. Special-purpose glass fibers make up a very small percentage of the total synthetic vitreous fibers produced in the United States, accounting for only about 1% of the total annual production (Carey 2004). In the United States, there are at least four companies that produce special-purpose glass fibers.

The United States International Trade Commission reports information on imports and exports of glass fibers only by cost. The combined value of imports of insulation products consist of the five product categories: (1) mats, nonwoven, of glass fibers, (2) thin sheets (voiles), nonwoven, of glass fibers, (3) batts of nonwoven glass fibers, (4) pipe coverings of nonwoven glass fibers, and (5) other insulation products of nonwoven glass fibers, which varied considerably between 2000 and 2008 with a maximum value of $356 million in 2006 and a minimum value of $189 million in 2001; the value for 2008 was $196 million (USITC 2009a). The value of exports for the product category "insulation products of glass fibers" increased steadily from $59 million in 2000 to $121 million in 2008 (note that the product categories differ for imports and exports) (USITC 2009b). No category for special-purpose fibers was identified for imports or exports.

Exposure

Depending on the production process, fibers can have relatively large or small diameters, which is important, because very thin fibers can enter the respiratory tract and deposit deep in the lungs. As noted above, the nominal diameter is an estimate of the average fiber diameter of the wool product; however, within that product, the diameters of individual fibers vary widely around the nominal diameter, and all wool products contain some percentage of respirable fibers (ACGIH 2001). Because smaller fibers become airborne more easily, the average diameter of airborne fibers will be smaller than the nominal diameter of the product. (Krantz 1988, ACGIH 2001). Krantz (1988) assessed exposure levels in nine Swedish factories that produced insulation wools (rock or glass) and special-purpose fibers and noted that for both insulation wools and special-purpose fibers the maximum median diameter for airborne glass fibers was less than 1 μm. When this value was compared with the nominal fiber diameter of the product, the distribution of airborne fiber diameters was smaller.

Analytical data from glass fiber manufacturing operations generally show higher air levels for the production of smaller diameter (special-purpose) fibers compared with larger diameter (insulation) fibers (NTP 2009). In a U.S. study of both insulation glass fibers and special-purpose fibers, Dement (1975) concluded that fiber concentrations in small-diameter fiber operations were many orders of magnitude higher than concentrations seen in larger diameter [insulation-wool] fiber operations, and in addition, the smaller diameters and shorter lengths make more fibers respirable. Data reported by

NTP (2009) show airborne fiber levels rarely exceed 1 fiber/cm^3 for insulation wool products; however, for small-diameter (special-purpose) fibers, this level often is exceeded.

Nonmanufacturing occupational exposures can occur while installing, removing, fabricating, or otherwise working with glass wool outside the manufacturing environment. Exposures in these end-user applications are typically higher than in the fiber manufacturing environments. Residential homeowners engaged in home remodeling projects potentially are exposed to insulation materials through the removal and replacement of existing products; however, no data were identified regarding the number of individuals involved in these activities or exposure levels.

For insulation installation activities, exposure levels vary depending on the insulation product and the task performed. Lees *et al.* (1993) conducted a comprehensive residential insulation installation exposure survey in the early 1990s. Workers were monitored during insulation operations in 107 houses in 11 different states. Respirable fiber concentrations during installation of glass wool batt insulation in homes ranged from 0.02 to 0.42 fibers/cm^3, with a mean of 0.14 fibers/cm^3. The installation of loose fiberglass insulation that had a binder resulted in mean exposures of 0.55 fibers/cm^3 for the installer and 0.18 fibers/cm^3 for the feeder. The highest exposures were noted for installation of loose insulation without binder. For installers, exposure levels ranged from 1.32 to 18.4 fibers/cm^3, with a mean of 7.67 fibers/cm^3, while for feeders, levels ranged from 0.06 to 9.36 fibers/cm^3, with a mean of 1.74 fibers/cm^3.

Data on exposures during glass wool removal are limited, but exposure levels appear to be less than those associated with installation, resembling levels seen in fiber manufacturing operations (Yeung and Rogers 1996).

Data from the latest U.S. Economic Census (USCB 2005) indicate that in 2002, there were 19,318 workers (15,788 in manufacturing) employed within the North American Industrial Classification System (NAICS) code 327993, which "comprises establishments primarily engaged in manufacturing mineral wool and mineral wool (i.e., fiberglass) (*sic*) insulation products made of such siliceous materials as rock, slag, and glass or combinations thereof." (Based on the proportions of glass wool to other mineral wools used in the production of insulation products in North America, it is likely that the majority of the workers are involved in the manufacture of glass fibers.)

As cited by Maxim *et al.* (2003), the U.S. Department of Labor (USDOL) Bureau of Labor Statistics (BLS 2009), reported approximately 53,000 workers were employed by insulation contractors in the year 2000. This number was projected to grow to 60,000 by 2010. In May 2007, the U.S. Bureau of Labor Statistics reported that nearly 31,000 workers were employed as "insulation workers" within the NAICS code 238310 (Drywall and Insulation Contractors). Additionally, workers involved in other construction trades such as drywall installers, carpenters, and heating and cooling specialists also install insulation. Approximately 150,000 of these workers have periodic exposure to glass wool insulation materials (Maxim *et al.* 2003). OSHA estimates that in 1992, 185,000 full-time-equivalent construction workers were employed in the U.S. residential insulation trades (cited by Lees *et al*. 1993). Esmen *et al.* (1982) reported that average respirable fiber exposure of workers for all applications, except the blowing of thermal insulation into attics, ranged from 0.003 to 0.13 fibers/cm^3. Average respirable glass wool exposure levels for various tasks during blowing attic insulation ranged from

0.31 to 1.8 fibers/cm^3. The range of individual exposure levels for the blower (the task with the highest exposure levels) was 0.67 to 4.8 fibers/cm^3.

No information was identified on environmental occurrence and exposure levels of specific glass fiber products (NTP 2009). In indoor environments, the available data suggest that airborne concentrations of glass fibers do not increase significantly after installation of insulation or due to air passing through ducts lined with glass fibers.

Regulations

U.S. Environmental Protection Agency (EPA)

Clean Air Act

National Emissions Standards for Hazardous Air Pollutants: Fine mineral fiber emissions from facilities manufacturing or processing glass (of average diameter ≤ 1 μm) is listed as a hazardous air pollutant.

New Source Performance Standards: Manufacturers of wool fiberglass are subject to provisions for the control of particulates as prescribed in 40 CFR 60.292 and 293.

Occupational Safety and Health Administration (OSHA)

Permissible exposure limit (PEL) = 15 mg/m^3 (total); 5 mg/m^3 (respirable) (based on regulation for "particulates not otherwise regulated").

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) limit = 1 fiber/cm^3 (respirable fibers).

National Institute for Occupational Safety and Health (NIOSH)

Recommended exposure limit (REL) = 3 fibers/cm^3 (TWA) (fibers with diameter ≤ 3.5 μm and length ≥ 10 μm); 5 mg/m^3 (TWA) (total) (listing is for "fibrous glass dust").

Occupational Safety and Health Administration (OSHA)

Health and Safety Partnership Program for Manufacturers: Maximum concentration of 1 WHO fiber/cc (cm^3), 8-hour TWA for respirable SVF (WHO fiber is a fiber with diameter < 3 μm, length ≥ 5 μm and length to diameter ratio ≥ 3:1).

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